AMENDMENT TO THE SPECIFICATION

Please replace paragraphs [0021]-[0070] with the following amended paragraphs:

[0021] The present invention comprises a compound for modulating kinase activity, particularly Tie-2, of Formula I,

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is a five- to six-membered aromatic ring system containing between one and three heteroatoms, said five- to six-membered aromatic ring system substituted with -X and -Y-L-Z, in an ortho relationship to each other, and said five- to six-membered aromatic ring system optionally substituted with up to four R¹;

each R^1 is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, -OC(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted lower heterocyclylalkyl;

optionally two of R^1 , together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of R^1 ;

X is selected from the following six formulae:

$$(R^{2})_{q} \xrightarrow{N} h_{p} \qquad (R^{2})_{q} \xrightarrow{N} h_{p} \qquad (R^{2})_{q} \xrightarrow{N} h_{p}$$

$$(R^{2})_{q} \xrightarrow{N} h_{p} \qquad (R^{2})_{q} \xrightarrow{N} h_{p}$$

$$(R^{2})_{q} \xrightarrow{N} h_{p} \qquad (R^{2})_{q} \xrightarrow{N} h_{p}$$

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312-913-0001

Preliminary Amendment Appl. No.: 10/549,300 Attorney Docket No. 05-934-F January 31, 2007 wherein.

W is selected from
$$-C(R^2)(R^2)$$
-, $-N(R^4)$ -, $-S(O)_{0.2}$ -, and $-O$ -;
 $n = 1$ or 2;
 $p = 0$ or 1;
 q is 1 to 3;
M is $-OR^3$ or $-N(R^3)R^4$:

each R^2 is independently selected from -H, halogen, oxo, -CN, -NH₂, -NO₂, -OR³, -N(R^3) R^3 , -N(R^3) R^5 , -S(O) $_{0.2}R^3$, -SO $_{2.2}N(R^3)R^3$, -CO $_{2.2}R^3$, -CO(O)N(R^3) R^3 , -N(R^3)SO $_{2.2}R^3$, -N(R^3)C(O)N(R^3) R^3 , -CO(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

two of R², together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each R^3 is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of R³, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each R^4 is independently selected from R^3 , $-SO_2R^3$, $-SO_2N(R^3)R^3$, $-CO_2R^3$, $-C(O)N(R^3)R^3$, and $-C(O)R^3$;

Y is selected from -CH2-, -O-, -S(O)0-2-, -N(R3)-, and absent;

L is selected from $-(CH_2)_{1:3}$, $-(CH_2)_{1:3}$ N(R^3), $-(CH_2)_{1:3}$ O-, $-(CH_2)_{1:3}$ S(O)₀₋₂- and absent; each of the aforementioned methylenes optionally substituted:

Z is a five- to seven-membered ring system or $-R^3$, said five- to seven-membered ring system optionally substituted with zero to four of R^5 ; and

Proliminary Amendment 3 Proliminary Amendment**

 R^5 is selected from -H, halogen, -CN, oxo, -NO₂, -OR³, -N(R³)R⁴, -S(O)_{0.2}R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

optionally two of R⁵, together with the atoms to which they are attached, form a second ring system fused with said five- to seven-membered ring system, said second ring system substituted with zero to four of R⁵, hereinafter embodiment [0021].

[0022] In one example, the compound is according to embodimentparagraph [0021], having formula II.

wherein, A and E are each independently N or $-C(R^1)$ -; and G is selected from $-S(O)_{0-2}$ -, and $-C(R^1)$ - $C(R^1)$ -, hereinafter embodiment [0022].

[0023] In another example, the compound is according to embodimentparagraph [0022], wherein Ar is selected from the following formulae-:

$$\bigvee_{(R^1)_{0\cdot 2}} \bigvee_{(R^1)_{0\cdot 4}} \bigvee_{(R^1)_{0\cdot 3}} \bigvee_{($$

hereinafter embodiment [0023].

[0024] In another example, the compound is according to embodimentparagraph [0023], wherein

-Y-L-Z is selected from the following formulae,

wherein g is zero to two; D is selected from $-C(R^5)(R^5)$ -, -O-, $-S(O)_{0:2^-}$, and $-N(R^4)$ -; Q is =N- or $-C(R^5)$ -, T is selected from absent, $-N(R^3)$ -, -S- and -O-; and each methylene between Y and T is optionally substituted; provided that when both Y and T are heteroatoms then g must be two hereinafter embodiment [0024].

[0025] In another example, the compound is according to embodimentparagraph [0024], wherein Y is -O- or optionally substituted -CH₂-, hereinafter embodiment [0025].

[0026] In another example, the compound is according to embodimentparagraph [0025], wherein X is selected from the following formulae:

hereinafter embodiment [0026]

[0027] In another example, the compound is according to embodimentparagraph [0026], wherein R^{4a} is selected from -SO₂R³, -SO₂N(R³)R⁴, -CO₂R³, -C(O)N(R³)R⁴, and -C(O)R³, hereinafter embodiment [0027].

[0028] In another example, the compound is according to embodimentparagraph [0027], wherein each R² is independently selected from -H or optionally substituted lower alkyl, hereinafterembodiment [0028].

[0029] In another example, the compound is according to embodimentparagraph [0028], wherein each R² is independently selected from -H, haloalkyl, -C_{1.6}alkyl-N(R³)R³, -C_{1.6}alkyl-CO₃R³, and -C_{1.6}alkyl-C(O)N(R³)R³, hereinafter embodiment [0029].

[0030] In another example, the compound is according to embodimentparagraph [0029], wherein R^{4a} is -C(O)N(R³)R³ or -C(O)R³, hereinafter embodiment [0030].

[0031] In another example, the compound is according to embodimentparagraph [0030], wherein -Y-L-Z is selected from the following formulae,

wherein Y, T, and g are as described above, hereinafter embodiment [0031].

[0032] In another example, the compound is according to embodimentparagraph [0031], wherein g is one or two, hereinafter embodiment [0032].

[0033] In another example, the compound is according to embodimentparagraph [0032], wherein each R^5 is independently selected from -H, halogen, -CN, -NH₂, -NO₂, -OR³, -N(R³)R⁴, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted lower alkyl, hereinafter embodiment [0033].

[0034] In another example, the compound is according to embodimentparagraph [0033], wherein -Y-L-Z is selected from the following formulaes:

hereinafter embodiment [0034]

[0035] In another example, the compound is according to embodimentparagraph [0034], having formula III.

$$\mathbb{R}^{3a}$$
 \mathbb{R}^{3b}
 \mathbb{R}^{3b}
 \mathbb{R}^{3b}
 \mathbb{R}^{3b}
 \mathbb{R}^{4b}

wherein J is N or CH, and B is =N- or =C(R⁵)-, hereinafter embodiment [0035].

[0036] In another example, the compound is according to embodimentparagraph [0035], wherein R^{3a} is selected from optionally substituted aryl, optionally substituted lower arylalkyl, optionally

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substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl, hereinafter embodiment [0036].

[0037] In another example, the compound is according to embodimentparagraph [0036], wherein R^{3a} is selected from optionally substituted aryl and optionally substituted heteroaryl, hereinafter embodiment [0037].

[0038] In another example, the compound is according to embodimentparagraph [0037], wherein R^{3a} is ontionally substituted phenyl, hereinafter embodiment [0038].

[0039] In another example, the compound is according to embodimentparagraph [0038], wherein said optionally substituted phenyl is substituted with at least one of halogen, -CN, -CF₃, -NH₂, -NO₂, -OR³, -N(R³)R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)COO)R³, -N(R³)COO)R³, -C(O)R³, optionally substituted lower alkyl, and optionally substituted aryl, hereinafter embodiment [0039].

[0040] In another example, the compound is according to embodimentparagraph [0039], wherein said optionally substituted phenyl group is substituted with at least one trifluoromethyl group, hereinafter embodiment [0040].

[0041] In another example, the compound is according to embodimentparagraph [0040], wherein said optionally substituted phenyl group is substituted with at least two trifluoromethyl groups, hereinafter embodiment [0041].

[0042] In another example, the compound is according to embodimentparagraph [0039], wherein said optionally substituted phenyl group is substituted with at least one lower alkyl groupahereinafter embodiment [0042].

[0043] In another example, the compound is according to embodimentparagraph [0039], wherein R^{3b} is -H, hereinafter embodiment [0043].

[0044] In another example, the compound is according to embodimentparagraph [0043], wherein R^{4b} is selected from R³, -H, -CO₂R³, -C(O)N(R³)R⁴, and -C(O)R³, hereinafter embodiment [0044].

[0045] In another example, the compound is according to embodimentparagraph [0044], wherein Ar is according to the formula below, hereinafter embodiment [0045].



[0046] In another example, the compound is according to embodimentparagraph [0044], wherein Ar is according to the formula below, hereinafter embodiment [0046].

$$\sqrt{N}$$

[0047] In another example, the compound is according to embodimentparagraph [0044], wherein Ar is according to the formula below, hereinafter embodiment [0047].

$$\langle \cdot \rangle$$

[0048] In another example, the compound is according to embodimentparagraph [0044], wherein Ar is according to the formula below, hereinafter embodiment [0048].

$$\langle \cdot \rangle$$

[0049] In another example, the compound is according to embodimentparagraph [0044], wherein Ar is according to the formula below, hereinafter embodiment [0049].

$${}$$

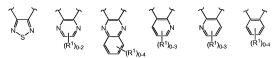
[0050] In another example, the present invention comprises a compound for modulating kinase activity, particularly Tie-2, of Formula IV,

$$(R^6)_{0.5} \bigwedge_{\text{Ar}}^{\text{HN}} \bigvee_{\text{R}^{2}} (R^2)_{0.4} \bigvee_{\text{B}}^{\text{R}^{40}}$$

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or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is selected from the following formulae:



 $-SO_2N(R^3)R^3$, $-CO_2R^3$, $-C(O)N(R^2)R^3$, $-N(R^3)SO_2R^3$, $-N(R^3)C(O)R^3$, $-N(R^2)CO_2R^3$, $-C(O)R^3$, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; optionally two of R^1 , together with the atoms to which they are attached, form a first ring system

each R¹ is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)_{0.2}R³,

optionally two of R', together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of R¹;

each R^2 is independently selected from -H, halogen, oxo, -CN, -NH₂, -NO₂, -OR³, -N(R^3)R³, -N(R^3)R⁵, -S(O)₀₋₂R³, -SO₂N(R^3)R³, -CO₂R³, -C(O)N(R^3)R³, -N(R^3)SO₂R³, -N(R^3)C(O)R³, -N(R^3)C(O)N(R^3)R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted lower heterocyclylalkyl;

two of R², together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each R^3 is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of R³, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each R^4 is independently selected from R^3 , $-SO_2R^3$, $-SO_2N(R^3)R^3$, $-CO_2R^3$, $-C(O)N(R^3)R^3$, and $-C(O)R^3$;

Y is selected from optionally substituted -CH₂-, -O-, -S-, and -N(R³)-;

L is selected from optionally substituted -CH2-, -O-, -S-, -N(R3)- and absent;

provided that Y and L are not both heteroatoms;

B is =N- or =C(H)-;

at each instance, R^5 and R^6 are independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R⁴, -S(O)_{0.2}R³, -SO₂N(R³)R², -CO₂R³, -C(O)N(R³)R, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

optionally two of R^5 , together with the atoms to which they are attached, form a ring system fused with the ring containing B according to formula IV, said ring system substituted with zero to two additional of R^5 , hereinafter embodiment [0050].

[0051] In another example, the compound is according to embodimentparagraph [0050], wherein Y is -O- and L is optionally substituted -CH_{2**} hereinafter embodiment [0051].

[0052] In another example, the compound is according to $\underline{embodimentparagraph}$ [0051], wherein at least one of R^6 is optionally substituted lower alkyl, $\underline{hereinafter\ embodiment\ [0052]}$.

[0053] In another example, the compound is according to embodimentparagraph [0052], wherein said at least one optionally substituted lower alkyl is meta- to the piperazine urea function as depicted in formula IV, hereinafter embodiment [0053].

[0054] In another example, the compound is according to embodimentparagraph [0053], wherein R^{4a} is selected from R^3 , -H, -CO₂ R^3 , -C(O)N(R^3) R^4 , and -C(O) R^3 , hereinafter embodiment [0054].

[0055] In another example, the compound is according to embodimentparagraph [0054], wherein R^{4a} is selected from -H, -CO₂R³, -C(O)N(R³)R⁴, and -C(O)R³, hereinafter embodiment [0055].

[0056] In another example, the compound is according to embodimentparagraph [0055], wherein

[0057] In another example, the compound is according to embodimentparagraph [0056], wherein Ar is according to the formula below, hereinafter embodiment [0057].

$$\sum_{N \leq N}$$

[0058] In another example, the compound is according to embodimentparagraph [0056], wherein Ar is according to the formula below, hereinafter embodiment [0058].

[0059] In another example, the compound is according to embodimentparagraph [0056], wherein Ar is according to the formula below, hereinafter embodiment [0059].

[0060] In another example, the compound is according to embodimentparagraph [0056], wherein Ar is according to the formula below, hereinafter embodiment [0060].

[0061] In another example, the compound is according to embodimentparagraph [0056], wherein Ar is according to the formula below, hereinafter embodiment [0061].



[0062] In another example, the compound is according to embodimentparagraph [0021], selected from Table 1, hereinafter embodiment [0062].

1	N-[(1R,2S)-2-phenylcyclopropyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	NH N
2	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
3	N-[4-chloro-3-(trifluoromethyl)phenyl]- 4-{4-((pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C Cl
4	N-[4-(1-methylethyl)phenyl]-4-{4- {(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	
5	N-(3-bromophenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	Br N N N N N N N N N N N N N N N N N N N
6	N-[3-(methylthio)phenyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl} piperazine-1- carboxamide	
7	N-(3-ethylphenyl)-4-{4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

8	N-(3,5-dimethylphenyl)-4-{4-[(pyridin- 4-ylmethyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	
9	N-[3-trifluoromethylphenyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
10	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {{(2-methylquinolin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
11	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[3- (dimethylamino)phenyl]methyl}oxy)- 1,2,5-thiadiazol-3-yl]piperazine-1- carboxamide	O N N N N N N N N N N N N N N N N N N N
12	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- (1H-indol-5-yloxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	F ₃ C CF ₃
13	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(3-thienylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N S
14	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(2-morpholin-4-ylethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃

15	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[2-(1H-imidazol-1-yl)ethyl]oxy}-1,2,5- thiadiazol-3-yl)piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
16	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(1-methylpiperidin-4-yl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃
17	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[4-(methyloxy)phenyl]methyl}oxy)- 1,2,5-thiadiazol-3-yl]piperazine-1- carboxamide	F ₃ C CF ₃
18	4-[4-({[3,4-bis(methyl]oxy)phenyl]methyl]oxy)- 1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-l- carboxamide	HN N N N N N N N N N N N N N N N N N N
19	4-{4-{(1,3-benzodioxol-5- ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N- [3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C CF ₃
20	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(furan-3-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
21	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(tetrahydrofuran-3-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃ O N N N N N N N N N N N N N N N N N N

22	N-[3,5-bis(trifluoromethyl)phenyl]-2- methyl-4-{4-([pyridin-4-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
23	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}-1,4-diazepane-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
24	1-{{[(1S,2R,5S)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy}acetyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
25	5-phenyl-N-(1-{4-[(pyridin-4- ylmethy])oxy]-1,2,5-thiadiazol-3- yl}pyrrolidin-3-yl)-1,3-oxazole-4- carboxamide	
26	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl},4-{[3- (trifluoromethyl)phenyl]acetyl}piperazi ne	F ₃ C N N N N N N N N N N N N N N N N N N N
27	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(piperidin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N NH
28	N-[3,5-bis(trifluoromethyl)phenyl]-N'- [(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperidin-4- yl)methyl]urea	F ₃ C CF ₃

29	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(3-pyridin-3-ylpropyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃
30	N-[3,5-bis(trifluoromethyl)phenyl]-4- {1,1-dioxido-4-[(pyridin:4- ylmethyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃ N N N N N N N N N N N N N N N N N N N
31	4-[4-(1-azabicyclo[2.2.2]oct-3-yloxy)- 1,2,5-thiadiazol-3-yl]-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
32	4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]benzoic acid	F_3 C CF_3 $N-S'$ CO_2 H
33	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(piperidin-3-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N NH
34	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(2-pyrrolidin-1-ylethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃
35	4-{4-[(2-amino-2-methylpropyl)oxy]- 1,2,5-thiadiazol-3-yl}-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C CF ₃ NH ₂

36	N-[3,5-bis(trifluoromethyl)phenyl]-1- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperidine-4- carboxamide	HN ON NO
37	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}-N-[3- (trifluoromethyl)phenyl]piperidine-4- carboxamide	HN N N N N N N N N N N N N N N N N N N
38	N-[3,5-bis(trifluoromethyl)phenyl]-4- {3-[(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}piperazine-1-carboxamide	F ₃ C CF ₃
39	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin- 2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
40	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(2-piperidin-4-ylethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃ N-S N H
41	2-methyl-4-{4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N- [3-(trifluoromethyl)phenyl]piperazine-1- carboxamide	O N N N N N N N N N N N N N N N N N N N
42	l-phenyl-4-{4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine	

43	1-[(4-methylphenyl)methyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine	N N N N N N N N N N N N N N N N N N N
44	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)amino]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃ HN N N N N N N N N N N N N N N N N N N
45	4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}-N-[3- (trifluoromethyl)phenyl]-1,4-diazepane- 1-carboxamide	O HN N CF ₃
46	2-methyl-1-{[2- (methyloxy)phenyl]carbonyl}-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl} piperazine	N N N N N N N N N N N N N N N N N N N
47	N-[5-chloro-2-(methyloxy)phenyl]-N'- (1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}pyrrolidin-3-yl)urea	
48	N-[5-methyl-2-(methyloxy)phenyl]-N'- (1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}pyrrolidin-3-yl)urea	
49	N-(1-{4-[(pyridin-4-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)- N'-[3-(trifluoromethyl)phenyl]urea	HN N N N

18

50	2-methyl-N-[4-(1-methylethyl)phenyl]- 4-{4-((pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HNN-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
51	2-methyl-N-[3-(methylthio)phenyl]-4- {4-[(pyridin-4-ylmethyl)xxy]-1,2,5- thiadiazol-3-yl}piperazine-1- earboxamide	
52	(2R)-N-[3,5- bis(trifluoromethyl)phenyl]-2-methyl-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C P ₃ P _N
53	(2R)-2-methyl-4-{4-{(pyridin-4- ylmethyl)oxy}-1,2,5-thiadiazol-3-yl}-N- [3-(trifluoromethyl)phenyl]piperazine-1- carboxamide	CF3 ON NATIONAL PROPERTY OF THE PROPERTY OF TH
54	1-[4-(4-[4-[(pyridin-4-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazin-1- yl)phenyl]ethanone	
55	2-(4-{4-[(pyridin-4-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazin-1- yl)pyrimidine	

56	1-[2-nitro-4-(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine	F ₃ C - NO ₂ N N N N N N N N N N N N N N N N N N N
57	(2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4- {4-((pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	F ₃ C-CF ₃ N N N N N N N N N N N N N N N N N N N
58	(2S)-2-methyl-4-{4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N- [3-(trifluoromethyl)phenyl]piperazine-1- carboxamide	HN-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
59	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- hydroxypyrazin-2-yl)piperazine-1- carboxamide	CF ₃
60	2-[2,5-bis(trifluoromethyl)phenyl]-N-(1- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}pyrrolidin-3- yl)acetamide	F ₃ C CF ₃ N N N N N N N N N N N N N N N N N N N
61	l-{[2,5-bis(trifluoromethyl)phenyl]acetyl}-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	F ₃ C N N N N N N N N N N N N N N N N N N N

62	N-[3,5-bis(trifluoromethyl)phenyl]-2- methyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- l-carboxamide	HN N N N N N N N N N N N N N N N N N N
63	2-methyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	O N N N N N N N N N N N N N N N N N N N
64	N-[3,5-bis(trifluoromethyl)phenyl]-2,6- dimethyl4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-earboxamide	CF ₃
65	2,6-dimethyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
66	N-(1-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3- yl)-N'-[3-(trifluoromethyl)phenyl]urea	F ₃ C N N N N
67	N-[3,5-bis(trifluoromethyl)phenyl]-N'-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)urea	F ₃ C CF ₃
68	N-[3,5-bis(trifluoromethyl)phenyl]-2,6- dimethyl-4-{4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N

69	2,6-dimethyl-4-{4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N- [3-(trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
70	N-[3,5-bis(trifluoromethyl)phenyl]-3- methyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
71	3-methyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
72	N-[3,5-bis(trifluoromethyl)phenyl]-4- {2-[(pyridin-4- ylmethyl)oxy]phenyl}piperazine-1- carboxamide	CF3 ON N
73	4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}- N-{3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
74	N-[3,5-bis(trifluoromethyl)phenyl]-2- methyl-4-{3-[(pyridin-4- ylmethyl)oxy]quinoxalin-2- yl}piperazine-1-carboxamide	PN N N N CF3

75	N-[3,5-bis(trifluoromethyl)phenyl]-4- {3-[(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}-1,4-diazepane-1-carboxamide	F ₃ C
76	2-methyl-4-{3-[(pyridin-4- ylmethyl)oxy quinoxalin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	N N N CF3
77	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin- 2-yl}-N-[3-(trifluoromethyl)phenyl]- 1,4-diazepane-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
78	N-[3,5-bis(trifluoromethyl)phenyl]-2,5- dimethyl4-{3-{(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-earboxamide	F ₃ C P ₃ C N N N N N N N N N N N N N N N N N N N
79	2,5-dimethyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	CF ₃
80	(2S)-N-[3,5- bis(trifluoromethyl)phenyl]-2-methyl-4- {3-[(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}piperazine-1-carboxamide	CF ₃
81	(2S)-2-methyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N

82	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-fluoropyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
83	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {((2-chloropyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F ₃ C NH N-N-S N N-S N N
84	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {((2-chloropyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- I-earboxamide	F ₃ C N N N N N N C I
85	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2- {[(2,3,5,6-tetrafluoropyridin-4- yl)amino]methyl}phenyl)piperazine-1- carboxamide	HN F CF3
86	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2- {[(3-chloro-2,5,6-trifluoropyridin-4- yl)amino]methyl}phenyl)piperazine-1- carboxamide	HN CI CF3

Table 1

87	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-bromopyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F ₃ C NH N N S
88	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-bromopyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- I-carboxamide	F ₃ C P ₃ P ₃ P ₃ P ₄ P ₅
89	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {((2-fluoropyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- 1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
90	N-[3,5-bis(trifluoromethyl)phenyl]-4- {5,6-dicyano-3-{(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- l-carboxamide	NC N
91	4-{5,6-dicyano-3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	NC N

92	N-(3-ethylphenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-carboxamide	
93	N-(3-ethylphenyl)-2-methyl-4-{3- [(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}piperazine-1-carboxamide	
94	N-(3-ethylphenyl)-2,6-dimethyl-4-{3- [(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}piperazine-1-carboxamide	
95	N-(3-ethylphenyl)-2-methyl-4-{3- [(pyridin-4-ylmethyl)oxy]quinoxalin-2- yl}piperazine-1-carboxamide	
96	N-[3,5-bis(trifluoromethyl)phenyl]-4-[3- (2-pyridin-4-ylethyl)pyrazin-2- yl]piperazine-1-carboxamide	F ₃ C CF ₃
97	N-[3,5-bis(trifluoromethyl)phenyl]-4- {3-[(pyridin-4-ylmethyl)oxy]pyridin-2- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

98	N-[3,5-bis(trifluoromethyl)phenyl]-4- {2-{(pyridin-4- yloxy)methyl]phenyl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
99	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
100	1,1-dimethylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbo nyl)piperazin-1-yl]-1,2,5-thiadiazol-3- yl}oxy)methyl]pyridin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
101	methyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
102	4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3- yl)oxy]methyl}pyridin-2-amine	H ₂ N N N N N N N N N N N N N N N N N N N
103	N-(4-chlorophenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine- 1-carboxamide	

104	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
105	N-(3-chlorophenyl)-4-{3-[(pyridin-4- ylmethyl)oxy]pyridin-2-yl}piperazine- 1-carboxamide	
106	4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}-N-propylpyridin-2-amine	HZ Z Z O O O O O O O O O O O O O O O O O
107	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(propylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
108	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(methylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

109	N-methyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	NH N-S
110	N-ethyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	TZ-s
111	N-butyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	NH ZZ-s
112	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(methylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
113	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(ethylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

114	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(butylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
115	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[{{2-[(phenylmethyl)amino]pyridin- 4-yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
116	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[{{2-[(1- methylethyl)painio]pyrimidin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
117	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2- [(phenylmethyl)amino]pyrimidin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃
118	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(phenylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

Table 1

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119	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[2- (dimethylamino)ethyl]amino}pyrimidin- 4-yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
120	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[2- (dimethylamino)ethyl]amino}pyridin-4- yl)methyl]oxy]-1,2,5-thiadiazol-3- yl)piperazine-1-earboxamide	N HN N N N N N N N N N N N N N N N N N
121	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(ethylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
122	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(propylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
123	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(cyclopropylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

124	4-[4-({[2-(acctylamino)pyrimidin-4-yl]mcthyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
125	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-{({{2^- [(phenylcarbonyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
126	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2- [(phenylcarbonyl)amino]pyrimidin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
127	4-{4-[({2- [bis(phenylcarbonyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3-yl}- N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C CF ₃

128	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(cyclopentylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N O O N N S' CF3 N S'
129	4-[4-({[2-(acetylamino)pyridin-4-yl]mcthyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C CF ₃
130	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[({[3,5- bis(trifluoromethyl)phenyl]amino}carbo nylamino]pyridin-4-yl}methyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C HN N N N N N N N N N N N N N N N N N N
131	methyl {4-[({4-[4-({[3,5-}bis(trifluoromethyl)phenyl]amino}carbo nyl)pipcrazin-1-yl]-1,2,5-thiadiazol-3- yl}oxy)methyl]pyrimidin-2- yl}carbamate	HN N N N N N N N N N N N N N N N N N N
132	4-(4-{[(2-aminopyridin-4- yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)- N-(3-ethylphenyl)piperazine-1- carboxamide	NH ₂

133	methyl [4-({[4-(4-{[(3- ethylphenyl)amino]earbonyl}piperazin- 1-yl)-1,2,5-thiadiazol-3- yl]oxy}methyl)pyridin-2-yl]carbamate	
134	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-cyanopyrimidin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	NC N
135	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
136	4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidine-2-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
137	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(butyloxy)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

138	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyrimidin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
139	4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)pipcrazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridine-2-carboxylicacid	HO HO N
140	2-pyrrolidin-1-ylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	N NH CF ₃ NH
141	2-morpholin-4-ylethyl {4-[({4-[4-({4-[4-({3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	N NH CF3
142	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

143	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-[[(1-methylpiperidin-3- yl)carbonyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	F ₃ C HN HN N
144	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-cthylphenyl)piperazine-1-carboxamide	S. N NH2
145	2-(4-methylpiperazin-1-yl)ethyl {4-[({4-[4,5,5-bis(trifluoromethyl)phenyl]amino}carbo nyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	NN NH CF3
146	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[(1-ethylpiperidin-4- yl)carbonyl]amino pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazino-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

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147	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-{3- [(trifluoromethyl)thio]phenyl}piperazin e-1-carboxamide	S-CF ₃ NH ₂ NH ₂ NH N N N N N N N N N N N N
148	4-({[4-(4-{[3,5-bis(trifluoromethyl)phenyl]sulfonyl}pip crazin-l-yl)-1,2,5-thiadiazol-3- yl]oxy}methyl)pyridin-2-amine	NH ₂ NH ₂ O=S CF ₃
149	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-naphthalen-1-ylpiperazine-1- carboxamide	N NH ₂ N NH N N N N N N N N N N N N N N N N N
150	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[{(2-[(N,N- dimethyl]pvyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	N N N N N N N N N N N N N N N N N N N
151	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[{{2-[(morpholin-4- ylacetyl)amino]pyridin-4- yl}methyloxyl-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

152	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[([2-[[piperidin-1- ylacetyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
153	ethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
154	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[{{2-[(pyrrolidin-1- ylacetyl)amino]pyridin-4- yl}methyl)oxyl-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
155	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {{[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy]-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
156	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(N,N- diethylglycyl)amino pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

157	1-ethylpiperidin-4-yl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbo nyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
158	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	NH ₂ N NH ₂ N N N O
159	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(2-oxo-1,3-oxazolidin-3-yl)pyridin- 4-yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
160	2-(diethylamino)ethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
161	methyl [4-({[2-(4-{[(3- ethylphenyl)amino]carbonyl}piperazin- 1-yl)pyridin-3-yl]oxy}methyl)pyridin-2- yl]carbamate	

162	2-pyrrolidin-1-ylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
163	2-piperidin-1-ylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbo nyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	O N N CF3 N N N CF3 N N N CF3
164	methyl [4-({[2-(4-{[(3- bromophenyl)amino]carbonyl}piperazin -1-yl)pyridin-3-yl]oxy}methyl)pyridin- 2-yl]carbamate	D D D D D D D D D D D D D D D D D D D
165	methyl {4-[({2-[4-({[3- (methyloxy)pheny)]amino}carbonyl)pip erazin-1-yl]pyridin-3- yl}oxy)methyl]pyridin-2-yl}carbamate	
166	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy pyridin-2-yl)-N-[3- (methyloxy)phenyl]piperazine-1- carboxamide	NH ₂ N N N N N N N N N N N N N N N N N N N

167	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy} pyridin-2-yl)-N-[3-(1- methylethyl)phenyl]piperazine-1- carboxamide	Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z
168	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-{3- [(trifluoromethyl)oxy]phenyl}piperazine -1-carboxamide	$\bigvee_{N \mapsto 1}^{N \mapsto 1} \bigvee_{N \mapsto 1}^{N \mapsto 1}^{N \mapsto 1} \bigvee_{N \mapsto 1}^{N \mapsto 1} \bigvee_$
169	4-(3-[[(2-aminopyrimidin-4- yl)methyl]oxyj pyridin-2-yl)-N-[2- fluoro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	NH2 N N N N N N N N N N N N N N N N N N
170	N-(3-ethylphenyl)-4-[3-({[2-({[(3-ethylphenyl)amino]carbonyl]amino)pyridin-4-yl]methyl}oxy)pyridin-2-yl]piperazine-1-earboxamide	HN NH N
171	N-(3-ethylphenyl)-4-(3-{[(2-{[(4- methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	NH NH NH

172	N-(3-ethylphenyl)-4-(4-{[(2-{[(4- methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	S-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
173	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- l-carboxamide	NH NH F ₃ C C _{F₃}
174	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy pyridin-2-yl)-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N NH
175	4-[3-({[2-(acetylamino)pyridin-4-yl]methyl}oxy)pyridin-2-yl]-N-(3-ethylphenyl)piperazine-1-carboxamide	NH NN NH NH
176	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-(3-ethyl- 4-fluorophenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

Table 1

177	2-[4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)piperazin-1-yl]-N-[3,5-bis(trifluoromethyl)phenyl]acetamide	N N N N N N N N N N N N N N N N N N N
178	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N- phenylpiperazine-1-carboxamide	H ₂ N N NH NH
179	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy] pyridin-2-yl)-N-(3- chloro-5-ethylphenyl)piperazine-1- carboxamide	H ₂ N N NH NH
180	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-(5-ethyl- 2-fluorophenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
181	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxyl pyridin-2-yl)-N-(3- bromo-5-ethylphenyl)piperazine-1- carboxamide	H ₂ N NH NH

Table 1

182	2-(4-methylpiperazin-1-yl)ethyl [4-({[2- (4-{[(3- ethylphenyl)amino]carbonyl}piperazin- 1-yl)pyridin-3-yl]oxyj methyl)pyridin-2- yl]carbamate	
183	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-chlorophenyl)piperazine-1-earboxamide	H ₂ N N N NH
184	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-bromophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
185	N-[4-({[2-(4-acctylpipcrazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]-2-(4-methylpipcrazin-1-yl)acctamide	>-N_N-N_N-N_N-N_N-N_N-N_N-N_N-N_N-N_N-N_
186	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
187	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(4-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

188	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
189	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
190	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}-5-bromopyridin-2-yl)- N-(3-ethylphenyl)piperazine-1- carboxamide	Br N N NH
191	N-methyl-4-(3-{[(2-{[(4- methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- I-carboxamide	NH NH NH
192	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-[2- chloro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
193	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy pyridin-2-yl)-N-(5- chloro-2-fluorophenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
194	4-(3-{[(2-amino-5-bromopyrimidin-4-yl)methyl]oxy]-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	Br N N NH

195	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-[2- fluoro-3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N NH NH CF ₃
196	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-[3- fluoro-5- (trifluoromethyl)phenyl]piperazine-1- earboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
197	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-(3,5- dichlorophenyl)piperazine-1- carboxamide	H ₂ N N NH NH
198	N-(3-chloro-5-ethylphenyl)-4-(3-{[(2- {[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- l-carboxamide	NH NH
199	N-(5-ethyl-2-fluorophenyl)-4-(3-{[(2- {[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- l-carboxamide	N NH NH NH
200	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-[3-ethyl- 5-(trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

201	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-(3- ethylphenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
202	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-(3- chloro-5-ethylphenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
203	4-(3-[{(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-(5- ethyl-2-fluorophenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
204	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N- methylpiperazine-1-carboxamide	H ₂ N N NH
205	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N- ethylpiperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
206	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N- cyclohexylpiperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
207	4-({[2-(4-acctylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine	Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z

208	4-({[2-(4-propanoylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin- 2-amine	Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z
209	N-(3-cyclopropylphenyl)-4-(3-{[(2- {[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	NH N
210	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-(3- cyclopropylphenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
211	N-[2-fluoro-5-(trifluoromethyl)phenyl]- 4-(3-{[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N N N N N N N N N N N N N N N N N N N
212	N-[3-fluoro-5-(trifluoromethyl)phenyl]- 4-(3-{[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- I-carboxamide	N N N N N N N N N N N N N N N N N N N

213	N-(3,5-dichlorophenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-l-carboxamide	NH NH NH
214	4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino] pyridin-4-yl)methyl]oxy} pyridin-2-yl)-N-(3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	NH NH F ₃ C
215	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-earboxamide	H ₂ N N N NH NH
216	4-(3-{[1-(2-aminopyrimidin-4- yl)ethyl]oxy] pyridin-2-yl)-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
217	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-(3,5- dichlorophenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
218	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-[3- fluoro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

219	4-[({2-[4-(3,4-dihydroquinolin-1(2H)-ylcarbonyl)pipcrazin-1-yl]pyridin-3-yl}oxy)methyl]pyrimidin-2-amine	N NH2
220	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-methylpropyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
221	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-(3-chloro-5-ethylphenyl)piperazine-1- carboxamide	S-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
222	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-(5-ethyl-2-fluorophenyl)piperazine-1- carboxamide	\$-N-N-N-NH N-N-N-NH N-N-N-NH
223	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-(3,5-dichlorophenyl)piperazine-1- carboxamide	S-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
224	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N- phenylpiperazine-1-carboxamide	H ₂ N N NH
225	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-[2- fluoro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

226	N-(3,5-diethylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)oxy]methyl}pyridin-2-yl)piperazine-1-carboxamide	NH NH
227	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}-6-methylpyridin-2-yl)- N-(3-ethylphenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
228	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}-6-methylpyridin-2-yl)- N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	H_2N F_3C F_3C
229	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
230	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-phenylpiperazine-1-earboxamide	S-N N NH
231	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	\$5-N N NH N F3C

232	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[2-fluoro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	9-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
233	N-[3-chloro-5-(trifluoromethyl)phenyl]- 4-(3-{[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- l-carboxamide	NH NH NH NH NH
234	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-[3- chloro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H_2N N F_3C CI
235	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-[3- chloro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
236	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyrazin-2-yl)-N-(3- bromo-5-ethylphenyl)piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
237	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy]-6-chloropyridin-2-yl)- N-(3-ethylphenyl)piperazine-1- carboxamide	CI N N NH

238	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	S-N N NH NH
239	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[3-fluoro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	\$-N_N NH N= NH NH NH
240	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[3-chloro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	\$-N_N NH N= F ₃ C CI
241	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy]pyrazin-2-yl)-N-(3- ethyl-4-fluorophenyl)piperazine-1- carboxamide	H ₂ N N NH NH
242	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	9-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
243	N-[3-chloro-2-fluoro-5- (trifluoromethyl)phenyl]-4-(3-{[(2-{[(4- methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N NH NH F3C CI

244	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	CI N N N N N N N N N N N N N N N N N N N
245	4-(3-{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH
246	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}-6-chloropyridin-2-yl)- N-(5-ethyl-2-fluorophenyl)piperazine-1- carboxamide	H ₂ N N N N N F
247	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-(3-ethyl- 5-fluorophenyl)piperazine-1- carboxamide	H ₂ N N NH
248	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	S-N-N-N-NH N-N-N-NH N-N-N-NH F3C-N-F
249	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy}pyridin-2-yl)-N-[3- chloro-2-fluoro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

250	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy} pyridin-2-yl)-N-[3,5- bis(trifluoromethyl)phenyl]-N- methylpiperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
251	4-(3-{[(2-aminopyrimidin-4- yl)methyl]oxy pyrazin-2-yl)-N-[3-(1- methylethyl)phenyl]piperazine-1- carboxamide	H ₂ N N NH NH
252	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-(3-ethyl-4-fluorophenyl)piperazine-1- carboxamide	S-N N NH
253	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-4-fluorophenyl)piperazine-1-carboxamide	9-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
254	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[2,5- bis(methyloxy)phenyl]piperazine-1- carboxamide	ş-N N NH NH
255	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy}phenyl)-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N NH NH NH CF ₃ C CF ₃
256	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy}phenyl)-N-(3- ethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH

257	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide	9-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
258	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-{3- [(trifluoromethyl)oxy]phenyl}piperazine-l-carboxamide	H ₂ N N NH
259	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide	S-N N NH
260	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H ₂ N NH NH CF ₃
261	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[3-(1-methylethyl)phenyl]piperazine- 1-carboxamide	S-N N NH
262	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[2-chloro-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	S-N N NH NH NH F3C
263	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-(3-fluorophenyl)piperazine-1- carboxamide	S-N N NH

264	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2-(ethyloxy)phenyl]piperazine-1-carboxamide	S-N-N-N-NH N-N-N-NH
265	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl)-N-(3,4-difluorophenyl)piperazine-1-carboxamide	H ₂ N NH NH
266	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[3-(methylthio)phenyl]piperazine-1- carboxamide	S-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
267	N-(3-acetylphenyl)-4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	S-N N NH
268	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy phenyl]-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
269	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-fluorophenyl)piperazine-1-carboxamide	H ₂ N N F NH
270	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy}phenyl)-N- phenylpiperazine-1-carboxamide	H ₂ N N NH

271	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy}phenyl)-N-(3,5- dichlorophenyl)piperazine-1- carboxamide	H ₂ N NH NH
272	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy]phenyl]-N-[3-fluoro-5- (trifluoromethyl]phenyl]piperazine-1- carboxamide	H ₂ N NH NH
273	4-[4-({[6,7-bis(methyloxy)quinolin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	\$-N_N NH NH NF ₃ C-CF ₃
274	4-({[4-(4-{[3,5-bis(trifluoromethyl)phenyl]acetyl}piper azin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyrimidin-2-amine	9-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
275	5-{[(2-aminopyrimidin-4- yl)methyl]oxy}-6-[4-({[3,5- bis(trifluoromethyl)phenyl]amino}carbo nyl)piperazin-1-yl]pyrazine-2- carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

276	4-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C — CF ₃
277	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy]-phenyl)-N-[3-ethyl-5- (trifluoromethyl)phenyl]piperazine-1- carboxamide	H ₂ N NH NH CF ₃
278	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy}phenyl)-N-(5-ethyl-2- fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
279	4-(2-{[(2-aminopyrimidin-4- yl)methyl]oxy}phenyl)-N-(3,5- diethylphenyl)piperazine-1-carboxamide	H ₂ N N N NH
280	4-[({4-[4-(naphthalen-2- ylacetyl)piperazin-1-yl]-1,2,5- thiadiazol-3-yl}oxy)methyl]pyrimidin- 2-amine	H ₂ N N N N
281	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH

[0063] Another aspect of the invention is a pharmaceutical composition comprising the compound according to any one of embodimentsparagraphs [0021]-[0062] and a pharmaceutically acceptable carrier, hereinafter embodiment [0063].

[0064] Another aspect of the invention is a metabolite of the compound or the pharmaceutical composition according to any one of embodiment[0064], hereinafter embodiment [0064].

[0065] Another aspect of the invention is a method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of a composition comprising at least one of the compound according to any of embodimentsparagraphs [0021]-[0062] and the pharmaceutical composition according to embodimentparagraph [0063], hereinafter embodiment [0065]

[0066] Another aspect of the invention is the method according to embodimentparagraph [0065], wherein the kinase is Tie-2, hereinafter embodiment [0066].

[0067] Another aspect of the invention is the method according to embodimentparagraph [0066], wherein modulating the *in vivo* activity of Tie-2 comprises inhibition of Tie-2.

[0068] Another aspect of the invention is a method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of a composition comprising at least one of the compound according to any of embodimentsparagraphs [0021]-[0062] and the pharmaceutical composition according to embodimentsparagraph [0063].

[0069] Another aspect of the invention is a method of screening for modulator of a Tie-2 kinase, the method comprising combining either a composition comprising at least one of the compound according to any of embodimentsparagraphs [0021]-[0062] and the pharmaceutical composition according to embodimentsparagraph [0063], and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.

[0070] Another aspect of the invention is a method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of at least one of the compound according to any of embodimentsparagraphs [0021]-[0062] and the pharmaceutical composition according to embodimentsparagraph [0063].